



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,063	03/26/2004	William Wold	INGN:106US	8527
32425 7590 08/08/2007 FULBRIGHT & JAWORSKI L.L.P. 600 CONGRESS AVE. SUITE 2400 AUSTIN, TX 78701			EXAMINER WHITEMAN, BRIAN A	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 08/08/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/810,063

Applicant(s)

WOLD ET AL.

Examiner

Brian Whiteman

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 1-22,39,40,42,48 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-38,41,43-47 and 49-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 5/25/07.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/25/07 has been entered.

Election/Restrictions

Claims 1-22, 39, 40, and 48 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and lung cancer, prostate cancer, ovarian cancer, testicular cancer, brain cancer, stomach cancer, uterine cancer, breast cancer, esophageal cancer, head & neck cancer, pancreatic cancer, liver cancer, kidney cancer, and blood cancer in claim 25 and 6.7K, RID-alpha, RID-beta, and 14.7K proteins in claim 41 and claim 42 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/15/06 and 5/2/06.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1635

Claims 50-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New matter rejection:

The limitation 'the vector comprises an E1B19K coding region' in new claims is not supported by the as-filed specification. There does not appear to be a written description of the claims limitation 'the vector comprises an E1B19K coding region' in the application as filed. See MPEP § 2163.06. Applicant cites page 54, lines 18-24 for support of the limitation. Page 54, lines 18-24 recite:

These results are similar to those obtained with VRX-013. That is, (i) infected cells express TRAIL, (ii) infected cells as indicated by expression of an adenovirus-coded protein (E1A in FIGS. 14 and 15) in general do not have apoptotic nuclei, possibly because they are protected from TRAIL-induced apoptosis by the Adenovirus E1B-19K anti-apoptotic protein, and (iii) uninfected cells neighboring the infected cells have apoptotic nuclei, presumably induced either by release of TRAIL from infected cells or because of direct contact with TRAIL expressed on the surface of infected cells.

The paragraph is directed to an observation with VRX-013 and VRX-014 and VRX-016 and a possible reason for why in vitro cells infected with VRX-013 did not have apoptotic nuclei. This paragraph is not directed to using E1B19K in an adenovirus vector comprising TRAIL coding region and ADP coding region for treating a genus of hyperproliferative diseases (cancer, metastatic cancer, recurrent cancer) or a method of rendering an inoperably tumor operable in a subject. Thus, nothing in the specification would lead one to the particular limitation set forth in the new claims. "It is not sufficient for purposes of the written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to

Art Unit: 1635

speculate as to modifications that the inventor might have envisioned, but failed to disclose.”

Lockwood v. American Airlines Inc., 41 USPQ2d 1961, 1966 (CAFC 1997).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1635

Claims 23-38, 41, 43-47, and 49-52 are rejected under 35 U.S.C. 103(a) as being obvious over Wold (US 6,627,190) taken with Walczak (C44).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The patent of Wold is directed to delivering to a tumor (colon) a replication competent adenovirus expressing adenovirus death protein. See column 86 and Figure 4. The adenovirus lacks the gp19k region (column 10). Wold teaches that the ADP coding region is under control of MLP promoter (column 6). Wold teaches that the adenovirus further comprises a mutation in the E1A region, said mutation impairing binding of E1A to p300 and/or pRB (column 86). Wold further teaches combination therapy with radiation (column 12). The adenoviral vectors taught

Art Unit: 1635

by Wold retain the E1b coding region comprising E1b19k region (columns 12-13). However, the Wold does not specifically teach expressing TRAIL from the adenovirus vector.

However, at the time the invention was made, TRAIL was known to one of ordinary skill in the art for its tumoricidal activity as taught by Walczak. See page 157. Walczak teaches a plasmid comprising TRAIL. See page 162.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wold taken with Walczak, namely to express ADP and TRAIL from the adenoviral vector in a tumor. One of ordinary skill in the art would have been motivated to combine the teaching because expressing TRAIL and ADP are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wold taken with Walczak, namely to use radiation therapy in combination with the adenovirus expressing ADP and TRAIL from the adenoviral vector in a tumor. One of ordinary skill in the art would have been motivated to combine the teaching because expressing radiation therapy and cancer gene therapy are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wold taken with Walczak, namely to express ADP and TRAIL from the E3 region of the adenovirus. One of ordinary skill in the

Art Unit: 1635

art would have been motivated to combine the teaching so that ADP and TRAIL are under control of the same promoter.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wold taken with Walczak, namely to express ADP and TRAIL from the MLP promoter in the E3 region of the adenovirus. One of ordinary skill in the art would have been motivated to combine the teaching so that ADP and TRAIL are under control of MLP promoter to have expression at the same time.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wold taken with Walczak, namely to use radiation therapy prior to, same time or after administration of the adenovirus expressing ADP and TRAIL. As a matter of designer's choice, one of ordinary skill in the art would have been motivated to combine the teaching to treat tumors in a mammal. The specification does not display any unexpected results when administering the second therapy prior to, same time, or after administration of the adenovirus.

In view of the teaching of Wold and Walczak, one of ordinary skill in the art would have a reasonable expectation of success for practicing the methods.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made

Applicant's arguments filed 5/25/07 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

Art Unit: 1635

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The Declaration under 37 CFR 1.132 filed 5/25/07 is insufficient to overcome the rejection of claims 23-38, 41, 43-47, and 49 based upon 103(a) as set forth in the last Office action because: See *In re Keller*. Furthermore, other than applicant's assertion that, "no particular suggestion or motivation to indicate that adenoviral vectors that express TRAIL and ADP can be successfully grown in cells lines or applies as in cancer therapy", applicant provide no evidence of record to support applicant's assertion. See *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisle* 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). The art of record teaches that replication competent adenoviral, ADP coding regions and TRAIL coding regions can be use to treat cancer in a subject. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Applicant argument that it is possible that expression of TRAIL may result in apoptosis of host cells infected with adenovirus, the argument is not found persuasive because the possibility of something happening does not support that one of ordinary skill in the art would not use the replication competent adenoviral vector for treating cancer in a subject. Furthermore, Tollefson et al. teaches that E1B19K inhibits killing of infected cells through TRAIL-induced apoptosis (C74). This allows, "prolong acute and persistent infections (page 8875)" of cells with adenovirus. In response to applicant's argument that Wold does not disclose vectors that express E1B19K and it is possible that expression of TRAIL in a vector of Wold could have resulted in apoptosis of infected cells, the argument is not found persuasive because applicant's assertion is not supported by any evidence of record. See *In re Schulze*. In addition, where, as here, the claimed and prior art products are identical or substantially

Art Unit: 1635

identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In *re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Furthermore Wold does not disclose deleting the E1B region of the adenovirus. This would indicate that E1b19k was intact in the adenovirus taught by Wold. In response to applicant's argument that Wold does not disclose unless and until actual studies are done to prepare adenovirus that include ADP and TRAIL coding regions and evaluate its efficacy in treating cancer, one of ordinary skill in the art would not be able to predict with any degree of certainty whether such a vector can be successfully applied to as an anticancer agent, the argument is not found persuasive because at the time of filing one of ordinary skill in the art could express two transgenes in a replication competent adenovirus (see Yu et al., US 7048920). In addition, see *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Furthermore, in response to applicant's argument, it is noted that the features upon which applicant relies (i.e., TRAIL coding region and ADP coding region operably linked to the adenovirus MLP promoter) are not recited in all of the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read

Art Unit: 1635

into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This is the case here since not all of the claims recite the limitation cited in applicant's argument.

Claims 23-38, 44-47 and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson (US 6,197,293) taken with Griffith et al. (US 6,900,185). Henderson teaches a replication competent adenovirus comprising the adenovirus death protein (ADP) (columns 42, 43, and 69). Henderson teaches using the adenovirus to treat cancer in humans (columns 1, 17, 29, and 33). Henderson teaches that radiation therapy is used to treat cancer (column 2). Henderson teaches that there is a need for adenoviral vectors that are better than replication defective adenovirus (column 5). Henderson further teaches that some types of cancers are resistant to conventional therapies usually used to treat cancer (column 2). The adenoviral vectors taught by Henderson retain the E1b coding region comprising E1b19k region (column 31). Henderson teaches that ADP can be under control of the E3 promoter or MLP promoter (columns 26-27). Henderson teaches using an additional transgene in the adenovirus (column 27). However, Henderson does not specifically teach expressing TRAIL from the adenovirus.

However, at the time the invention was made, Griffith teaches a method of treating cancer using an adenovirus comprising a promoter operably linked to a transgene encoding TRAIL (column 21). The cancer can be colon cancer (column 21). The cancer can be in a human (column 22). The method can further comprise administering a chemotherapeutic agent, radiotherapeutic agent, an immunomodulating agent (column 22).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Henderson taken with Griffith, namely to

Art Unit: 1635

express ADP and TRAIL from the adenoviral vector in a tumor. One of ordinary skill in the art would have been motivated to combine the teaching for enhancing the treatment of cancer cells in a subject because expressing TRAIL and ADP are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Henderson taken with Griffith, namely to use radiation therapy in combination with the adenovirus expressing ADP and TRAIL from the adenoviral vector in a tumor. One of ordinary skill in the art would have been motivated to combine the teaching because expressing radiation therapy and cancer gene therapy are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Henderson taken with Griffith, namely to express ADP and TRAIL from the E3 region of the adenovirus. One of ordinary skill in the art would have been motivated to combine the teaching so that ADP and TRAIL are under control of the same promoter.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Henderson taken with Griffith, namely to express ADP and TRAIL from the MLP promoter in the E3 region of the adenovirus. One of ordinary skill in the art would have been motivated to combine the teaching so that ADP and TRAIL are under control of MLP promoter to have expression at the same time.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Henderson taken with Griffith, namely to use radiation therapy prior to, same time or after administration of the adenovirus expressing ADP and TRAIL. As a matter of designer's choice, one of ordinary skill in the art would have been motivated to combine the teaching to treat tumors in a mammal. The specification does not display any unexpected results when administering the second therapy prior to, same time, or after administration of the adenovirus.

In view of the teaching of Henderson and Griffith, one of ordinary skill in the art would have a reasonable expectation of success for practicing the methods.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 5/25/07 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The Declaration under 37 CFR 1.132 filed 5/25/07 is insufficient to overcome the rejection of claims 23-38, 41, 43-47, and 49 based upon 103(a) as set forth in the last Office action because: See *In re Keller*. Furthermore, other than applicant's assertion that, "no particular suggestion or motivation to indicate that adenoviral vectors that express TRAIL and ADP can be successfully grown in cells lines or applies as in cancer therapy", applicant provide

Art Unit: 1635

no evidence of record to support applicant's assertion. See *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler* 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

The art of record teaches that replication competent adenoviral, ADP coding regions and TRAIL coding regions can be use to treat cancer in a subject. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Applicant argument that it is possible that expression of TRAIL may result in apoptosis of host cells infected with adenovirus, the argument is not found persuasive because the possibility of something happening does not support that one of ordinary skill in the art would not use the replication competent adenoviral vector for treating cancer in a subject. Furthermore, Tollefson et al. teaches that E1B19K inhibits killing of infected cells through TRAIL-induced apoptosis (C74). This allows, "prolong acute and persistent infections (page 8875)" of cells with adenovirus. In response to applicant's argument that Henderson does not disclose vectors that express E1B19K and it is possible that expression of TRAIL in a vector of Henderson could have resulted in apoptosis of infected cells, the argument is not found persuasive because applicant's assertion is not supported by any evidence of record. See *In re Schulze*. In addition, where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re*

Art Unit: 1635

Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Furthermore Henderson does not disclose deleting the E1B region just the E1B promoter of an adenovirus. This would indicate that E1b19k was intact in the adenovirus taught by Henderson. In response to applicant's argument that Henderson does not disclose unless and until actual studies are done to prepare adenovirus that include ADP and TRAIL coding regions and evaluate its efficacy in treating cancer, one of ordinary skill in the art would not be able to predict with any degree of certainty whether such a vector can be successfully applied to as an anticancer agent, the argument is not found persuasive because at the time of filing one of ordinary skill in the art could express two transgenes in a replication competent adenovirus (see Yu et al., US 7048920). In addition, see *In re Best*, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Furthermore, in response to applicant's argument, it is noted that the features upon which applicant relies (i.e., TRAIL coding region and ADP coding region operably linked to the adenovirus MLP promoter) are not recited in all of the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This is the case here since not all of the claims recite the limitation cited in applicant's argument.

Claims 23 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson (US 6,197,293) taken with Griffith et al. (US 6,900,185) as applied to Claims 23-38, 44-47 and 49 above, and further in view of Bruder et al. (Journal of Virology, 71:7623-7628, 1997).

Art Unit: 1635

Henderson taken with Griffith do not specifically teach using the adenovirus, wherein the gp19k region is deleted from the adenovirus.

However, at the time the invention was made, one of ordinary skill in the art understands that the adenovirus gp19K gene product associates with major histocompatibility complex class I proteins and prevents their maturation by sequestering them in the endoplasmic reticulum. The gp19K has been shown to block the ability of adenovirus-specific cytotoxic T lymphocytes to recognize virus-infected cells (page 7623).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Henderson taken with Griffith in further view of Bruder, namely to delete the gp19k region from the adenovirus. One of ordinary skill in the art would have been motivated to combine the teaching so that the mammal's immune system can recognize the adenovirus and assist in killing the tumor cells infected with the adenovirus.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 5/25/07 have been fully considered but they are not persuasive because the arguments were already addressed in the prior 103(a) rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Art Unit: 1635

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-26, 32-38, 41, 43-47 and 49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 18-46, and 56-75 of copending Application No. 11/057710. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to delivering to a tumor a replication competent adenovirus expressing adenovirus death protein and TRAIL. VRX-013 is used in the instant application working examples and is used in the method of the claims of '710.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed 5/25/07 have been fully considered but they are not persuasive for the reasons of record. It is noted that applicant will file a terminal disclaimer if necessary, once either application is allowed.

Claims 23-26, 32-34, 36-38, 41, 43-47 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-11 of U.S. Patent No.

Art Unit: 1635

6,627,190 in view of Walczak (C44). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to delivering to a tumor a replication competent adenovirus expressing adenovirus death protein. However, the claims from '190 do not specifically teach using expressing TRAIL from the adenovirus vector.

However, at the time the invention was made, TRAIL was known to one of ordinary skill in the art for its tumoricidal activity as taught by Walczak. See page 157. Walczak teaches a plasmid comprising TRAIL. See page 162.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of claims from '190 taken with Walczak, namely to express ADP and TRAIL from the adenoviral vector in a tumor. One of ordinary skill in the art would have been motivated to combine the teaching to enhance the treatment of a tumor in a subject because expressing TRAIL and ADP are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 5/25/07 have been fully considered but they are not persuasive.

Applicant argues that in view of MPEP 804 III limiting the use of issued patents to the claims, the combination of Wold and Walczak would not lead one to create a single replication competent adenoviral vector expressing ADP and TRAIL but instead would at most suggest the use of two vectors (one for each gene) with the latter being replication defective, the argument is

Art Unit: 1635

not found persuasive because in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The only difference between the instant claims and the claims of '190 is the claims from '190 do not recite using an additional transgene in the replication competent adenoviral vector. One of ordinary skill in the art would have been motivated to combine the teaching of Wold and Walczak to enhance the reduction of tumors in a subject because expressing TRAIL and ADP are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Also See *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970).

Claims 23-26, 32-38, 41, 43-47 and 49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-15, 20-22, 24, 32-44, 60-75, and 97-108 of copending Application No. 09/351,778 (C43) in view of Walczak (C44). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to delivering to a tumor a replication competent adenovirus expressing adenovirus death protein. However, the claims from '778 do not specifically teach using expressing TRAIL from the adenovirus vector.

However, at the time the invention was made, TRAIL was known to one of ordinary skill in the art for its tumoricidal activity as taught by Walczak. See page 157. Walczak teaches a plasmid comprising TRAIL. See page 162.

Art Unit: 1635

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of claims from '778 taken with Walczak, namely to express ADP and TRAIL from the adenoviral vector in a tumor. One of ordinary skill in the art would have been motivated to combine the teaching because expressing TRAIL and ADP are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 5/25/07 have been fully considered but they are not persuasive for the reasons of record. It is noted that applicant will file a terminal disclaimer if necessary, once either application is allowed.

Claims 23-26, 32-38, 41, 43-47 and 49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-72 of copending Application No. 11/249873 in view of Walczak (C44). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to delivering to a tumor a replication competent adenovirus expressing adenovirus death protein. However, the claims from '873 do not specifically teach using expressing TRAIL from the adenovirus vector.

Art Unit: 1635

However, at the time the invention was made, TRAIL was known to one of ordinary skill in the art for its tumoricidal activity as taught by Walczak. See page 157. Walczak teaches a plasmid comprising TRAIL. See page 162.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of claims from '873 taken with Walczak, namely to express ADP and TRAIL from the adenoviral vector in a tumor. One of ordinary skill in the art would have been motivated to combine the teaching because expressing TRAIL and ADP are well known to one of ordinary skill in the art for treating tumors. See *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

This is a provisional obviousness-type double patenting rejection.

Applicant's arguments filed 5/25/07 have been fully considered but they are not persuasive for the reasons of record. It is noted that applicant will file a terminal disclaimer if necessary, once either application is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 6:30 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Art Unit: 1635

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Brian Whiteman/
Primary Examiner, Art Unit 1635